REMARKS

Restriction Requirement:

Applicants elect to prosecute on the merits in this application the subject matter of Group I, claims 1-6 and 20-25, drawn to a glycated hemoglobin detection system. Applicant respectfully requests that the claims of Group I be examined. Claims 7-11, drawn to an analytical composition, claims 12-15, drawn to a method of making an analytical kit, claims 16-19, drawn to a method of preparing a sample, are canceled without prejudice, subject to the filing of a divisional application.

To avoid the use of trademarks and names used in trade as limitations in the claim language of the present invention, the identifications of the trademarks and the names used in trade appeared in the original application, including SURFYNOL®, PLURONIC®, TETRONIC®, ZWITTERGENT® 3-14; SURFYNOL® 400 series, including 440, 465 and 485, "L Series" EO-PO-EO, and "R Series" PO-EO-PO, are added into the specification at paragraphs 2 and 3 on page 9. All the information is well defined in the art and/or in the literatures from the manufactories, which have been submitted previously in the first IDS as listed below:

1. SURFYNOL® 400 Series, Liquid, Nonionic Surface-Active Agents SURFYNOL® 440, 465, 485, Air Products and Chemicals, Inc. Performance Chemicals (Product Brochure).

2. PLURONIC®, TETRONIC® Surfactants, BASF Corporation Specialty Products (Product Brochure). (The brochure also has definitions for both "L Series" EO-PO-EO and "R Series" PO-EO-PO).

Claims 1-6 and 20-25 are rejected under 35 U.S.C.§ 102(b) as allegedly being anticipated by *Hirai et. al.* (US5,882,935). This rejection is respectfully traversed.

Claims 1-6 and 20-25 of the present invention claim that a system comprises two elements: a device and a "sample dilution solution" which comprises a combination of two surfactants: the first for an analyte modification and the second for stability. The claimed features of the present invention, especially the sample dilution solution with two surfactants, are not shown or suggested

by *Hirai et. al.,* taken either alone or in any combination with other references. *Hirai et. al.,* disclosed only a diluent which has no more than one surfactant and the sole function of surfactant is hemolysis of an analyte as directly quoted below:

> "The *diluent* may be a buffer solution as well as purified water... *A* commercially available hemolysis agent or *surfactant* (for example, Triton X-100) may be used..." (*emphasis added*).

The discloser on Col 6, line 45-50, "Examples of the surfactant which may be used for the hemolysis agent include: ...and ampholytic ['zwitterionic']..." as emphasized by the Examiner, only provides further examples of surfactants which may be used as the hemolysis reagent in the diluent. Similarly to discussion above, Hirai et al. failed to show or suggest a sample dilution solution with a combination of two surfactants (one for an analyte modification and the other for stability). Additionally, *Hirai et. al.,* disclosed the surfactant only for hemolysis and failed to recognized or foresee the importance and impact of a stabilizing surfactant on the stability of the whole test system as discussed below.

As demonstrated in the present invention (Second paragraph on page 10), the stability or shelf life of a test system as a whole depends not only on the individual stability of the components of the test system, that is, the sample dilution solution and the device which contains dry reagent assay strips, but also on the interaction between these components. A test system with a stable sample dilution sample and a stable device having stable assay strips is most likely stable. However, a test system with unstable assay strips and stable sample dilution solution can still be stable as long as the sample dilution solution is able to provide an interaction that can correct or cancel the instability (*e.g.* interferences formed during storage) of the assay strips. That is the exact situation demonstrated in the present invention. When a device with assay strips were tested using a sample dilution solution with only modifying surfactant, the stability of the device was estimated to be about 3 to 7 days at 45°C (Figures 3-4). However, the stability of the same device was increased to about 3-4 months at 45°C when a second stabilizing surfactant was added into the sample dilution solution (Figures 5-8).

However, the general term of "surfactants" (Col. 11, line 20) recited by *Hirai et. al.,* on Col. 11, line 20 is to describe a possibility to "improve...reactivity and storage stability of" the "*substrate layer*" which forms part of an assay strip. This disclosure is limited to the substrate layer of the assay strip only but not the whole system or the diluent as disclosed in the present invention. Apparently, the scope of the stability is significantly different between *Hirai et. al.,* and the present invention. The stability recited in *Hirai et. al.* is limited to the stability of the assay strip whereas the stability in the present invention is related to the test system as a whole, the result of the interaction between a sample dilution solution and a device with the assay strips inside. The whole system with instable assay strips, thus an unstable device, can still be stable as long as the sample dilution solution can mediate the undesirable effects of the unstable device.

Claims 6 and 25 are rejected under 35 U.S.C.§ 103(a) as allegedly being unpatentable over *Hirai* (USP 5,882,935) in view of *Spring* (USP 5,643,721). This rejection is respectfully traversed.

Both claims 6 and 25 are amended to recite the dry reagent as part of the invention as suggested by the Examiner. As discussed above, Claims 6 and 25 recite a sample dilution solution comprising a combination of two surfactants. The stability of a system is affected by not only the stability of its components but also on the interaction of these components. By contrast, *Hirai et. al.* discloses that the diluent contains a single surfactant. Apparently, the teachings of *Hirai* do not disclose or suggest the recited invention, a system with, alone or in combination with *Spring*. Claims 6 and 25 are patentably distinguishable over the references.

<u>Table of Exemplary Support</u>

Claim Numb	**Claim Content**	**Explanation**
3	A system according to claim 1 wherein <u>the first surfactant is a nonionic surfactant and</u> the second surfactant is a ~~nonionic~~ <u>zwitterionic or an ionic</u> surfactant.	"The first and the second surfactants" are recited at 8:26-28.
6	The dry microparticulate is a latex particle	"Microparticlate" and "latex particle" are recited at 5:25.
22	A system according to claim 1 wherein <u>the first surfactant is a nonionic surfactant and</u>	"The first and the second

	the second surfactant is a ~~nonionic~~ zwitterionic or an ionic surfactant.	surfactants" are recited at 8:26-28.
25	The dry microparticulate is a latex particle	"Microparticlate" and "latex particle" are recited at 5:25.
26	The first surfactant is an ionic surfactant and the second surfactant is a zwitterionic or a nonionic surfactant	"The first and the second surfactants" are recited at 8:28-30.
27	The zwitterionic surfactant is N-hexadecyl-N,N-dimethyl-3-amino-1-propanesulfonate and the nonionic surfactant is an ethoxylated acetylenic glycol polymer or a block copolymer of ethylene oxide and propylene oxide.	An equivalent term for "N-hexadecyl-N,N-dimethyl-3-amino-1-propanesulfonate" is recited at 9:23 as "Zwittergent 3-14" and amended currently in the specification. "Ethoxylated acetylenic glycol polymer" is recited at 9:13. Equivalent terms for "a block copolymer of ethylene oxide and propylene oxide" is recited at 9:13-14 as PLURONIC® and TETRONIC®, and currently amended into the specification.
28	Ethoxylated acetylenic glycol is ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol.	An equivalent term for "Ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol" is recited at 9:10 as "SURFYNOL® and currently amended into the specification.
29	The ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol has an ethylene oxide content of from about 40 to about 85% by weight.	Equivalent terms for "about 40 to about 85%" are recited at 9:12 as "the 400 series, such as the 440, 465 and 485 products." The chemical compositions are defined in the manufactory brochure and amended currently into the specification.
30	The ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol has an ethylene oxide content of about 85% by weight.	An equivalent term for "85%" is recited at 10:14-16 as "SURFYNOL® 485."
31	The block copolymer of ethylene oxide and propylene oxide is a polyethylene oxide-polypropylene oxide- polyethylene oxide triblock copolymer or a polypropylene oxide-polyethylene oxide-	Equivalent terms "the triblock polymers" are recited at 9:15 as "L Series" EO-PO-EO and "R Series" PO-EO-PO. These two names used in trade are amended

	polypropylene oxide triblock copolymer.	currently into the specification.
32	The amount of the second surfactant in the blood dilution solution is from about 0.001% to 15% w/v.	The range is recited at 8:33.
33	The amount of the second surfactant in the blood dilution solution is from about 0.01% to 10% w/v.	The range is recited at 8:33.
34	The amount of the second surfactant in the blood dilution solution is from about 0.05% to 8% w/v.	The range is recited at 8:33.
35	The amount of the second surfactant in the blood dilution solution is from about 0.1% to 5% w/v.	The range is recited at 8:34.
36	The first surfactant is an ionic surfactant and the second surfactant is a zwitterionic or a nonionic surfactant	See claim 26.
37	The zwitterionic surfactant is N-hexadecyl-N,N-dimethyl-3-amino-1-propanesulfonate and the nonionic surfactant is an ethoxylated acetylenic glycol polymer or a block copolymer of ethylene oxide and propylene oxide.	See claim 27.
38	Ethoxylated acetylenic glycol is ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol.	See Claim 28.
39	The ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol has an ethylene oxide content of from about 40 to about 85% by weight.	See Claim 29.
40	The ethoxylated-2,4,7,9-tetramethyl-5-decyne-4,7-diol has an ethylene oxide content of about 85% by weight.	See Claim 30.
41	The block copolymer of ethylene oxide and propylene oxide is a polyethylene oxide-polypropylene oxide- polyethylene oxide triblock copolymer or a polypropylene oxide-polyethylene oxide-polypropylene oxide triblock copolymer.	See Claim 31.
42	The amount of the second surfactant in the blood dilution solution is from about	See Claim 32.

	0.001% to 15% w/v.	
43	The amount of the second surfactant in the blood dilution solution is from about 0.01% to 10% w/v.	See Claim 33.
44	The amount of the second surfactant in the blood dilution solution is from about 0.05% to 8% w/v.	See Claim 34.
45	The amount of the second surfactant in the blood dilution solution is from about 0.1% to 5% w/v.	See Claim 35.

SUMMARY

If the Examiner believes that it would facilitate prosecution, Applicants' Patent Agent, Lin Yu, Ph.D. may be contacted at (619) 230-7457 or at lyu@gordonrees.com.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-1990 and please credit any excess fees to such deposit account.

Respectfully submitted,

Dated: November 2, 2005

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